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10/517,653	03/08/2005	Adrian Keith West	47-217	5626

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EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/517,653	WEST ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-17,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-17 and 28* is/are rejected.

7)☒ Claim(s) *29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 20 August 2009 have been entered. Claims 1, 3-17, and 28-29 are pending and under examination.

Rejections Maintained and Necessitated by Amendment

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, and 13 are rejected under 35 U.S.C. 102(b) as anticipated by Penkowa 2002 (Journal of Comparative Neurology 444(2):174-189).

This rejection is maintained for the reasons of record and explained in further detail below. The teachings of Penkowa have been extensively discussed on the record. Briefly, the reference teaches administering MT-2, recited in claim 1, to mice. Some of the mice also had been treated with 6-AN, which damages the brain. Administration of MT-2 was via the intraperitoneal route (p. 184 end of first column). The specification explicitly states that this route of administration is sufficient to allow MT-2 to have its effects (p. 4 lines 6-10). The dose of MT-2 administered was 17.5 μg per mouse, split into three daily injections. Mice were given the MT-2 for up to three days (p. 176, end of first paragraph). As set forth previously, absent evidence to the contrary, it is presumed that the dose and duration of administration is sufficient to induce neurite outgrowth. Because the prior art reference teaches administration of the same product (here, MT-2) to the same patient population (here, living neurons), the recited effects must necessarily occur. See MPEP § 2112, 2112.01, and Ex Parte Novitski (26 USPQ 2d 1389). Note that the present specification states that *in vivo*, four days is sufficient to induce neurite outgrowth (p. 8 first two paragraphs, p. 9 final paragraph); Penkowa administered the drug for three days. The examiner is unable to determine if the dose used in the specification is exactly the same as that used in the reference by Penkowa, since the reference by Penkowa discloses the dose in terms of μg administered per unit of body weight, whereas the specification does not disclose the amount of MT-2 used *in vivo*; culture experiments only describe the final concentration of MT-2 in culture medium.

Applicant argues that the claimed invention cannot be anticipated by Penkowa. Applicant makes the following specific arguments, each of which will be answered in turn:

1) Protection and survival of neurons occurs 1-2 days after injury, whereas growth of new neurites occurs 4-7 days after injury (remarks, p. 5). Penkowa teaches a protective role of MT-2 against neural degeneration, not regenerative growth of neurons following MT-2 administration. According to applicant, this difference is reflected in the claims as presently written.

2) Detection of neurorpotection and detection of regenerative growth are completely different, and since Penkowa did not detect the latter he could not have possibly disclosed it was occurring.

3) The declaration filed by Dr. West provides evidence that the methods of Penkowa do not allow sufficient MT-2 to reach the brain, and since the claims require that "a sufficient amount of said metallothionein to stimulate said outgrowth of neurites" reach the neurons, the methods of Penkowa cannot possibly anticipate the claimed invention.

Applicant's arguments have been fully considered but they are not persuasive. With respect to 1) above, applicant is not claiming a certain time frame of administration. Independent claim 1, as written requires only a single step, namely administering MT-2 (or MT-I) to a living neuron. The claim does not require any particular time frame of administration. Even if it were later amended to require, for example, that the MT-2 be administered for a sufficient duration to achieve neurite outgrowth, Penkowa teaches administration of this protein for three days, which is very close to the range that applicant has described in the remarks as be sufficient to achieve "regenerative growth", which includes neurite outgrowth. Since Penkowa teaches administration of the same protein for the appropriate amount of time, the recited effect (stimulating outgrowth of neurites) must necessarily occur.

With respect to 2), whether or not the methods of detection of neurite outgrowth were performed by Penkowa is immaterial, since applicant is not claiming a step of detecting neurite outgrowth. Again, the only step is contacting the neurons with MT-2. The specification explicitly states that intraperitoneal injection, used by Penkowa, is an effective means to provide for the contacting step. As set forth in the interview between this examiner and Leonard Mitchard, applicant's representative, on 22 June 2009, if the claims were amended to include a step of measuring the degree of axonal growth, claims drawn to administration of MT-2 would likely be considered both novel and non-obvious over Penkowa and over Giralt (discussed below), as

those references discuss the effects of MT-2 on glia and on the immune system but do not suggest measuring axonal growth. However, applicant has chosen not to amend the claims to include such a step.

With respect to 3), the examiner acknowledges that the declaration shows that one figure shows that administration of 250 μg/10 g of body weight does not result in MT-2 appearing in the brain, and that another figure shows that the protein, when administered i.p., does enter the kidney. Ostensibly the second tissue (kidney) was taken as a positive control, i.e. to show that the test system is able to detect MT-2, suggesting that the first figure provides evidence in support of the assertion that MT-2 fails to enter the brain.

The declaration under 37 CFR 1.132 filed 20 August 2009 is insufficient to overcome the rejection of claim 1 based upon anticipation as set forth in the last Office action. The examiner of course does not challenge the data presented, but does not believe they support the conclusion that MT-2 enters the kidney but not the brain. The experiments are confounded, in that they were taken at two very different time points. The data showing that MT-2 enters the kidney were taken four days after administration of the protein, whereas the data showing that MT-2 does not enter the brain were taken 40 minutes after injection (see Exhibit 1, legends for Figures A and B). Applicant has interpreted these data as indicating that MT-2 enters the kidney but not the brain following peripheral (i.p.) administration. An equally parsimonious explanation is that MT-2 takes somewhere between forty minutes and four days to enter tissue following peripheral administration. There is no particular reason to believe that MT-2, when peripherally administered, cannot enter the brain within four days, especially given that applicant has stated that four days is an effective time frame (specification, p. 9, final paragraph) and that i.p. administration is an effective route of administration (specification, p. 4 second paragraph). Since the specification shows that following i.p. administration neurite outgrowth occurs between 18 hours and four days (specification, p. 8 final paragraph and p. 9 final paragraph), and since Penkowa teaches peripheral administration for three days (see Penkowa, p. 176 first paragraph, note injections were performed for three days, not 40 minutes as in the experiments presented in the declaration), neurite outgrowth would necessarily occur.

If applicant were to provide evidence that four days after MT-2 peripheral administration this protein is not found in the brain, such evidence may be sufficient to overcome the rejection over Penkowa for anticipation. However, that same evidence might raise questions about enablement, as the claims broadly encompass peripheral administration of MT-1 and MT-2.

For at least the reasons above, the rejection of claims 1 and 4 over Penkowa is maintained. Claim 4 is rejected as it recites a product-by-process limitation ("wherein said MT-IIA is produced by chemical synthesis or by production in genetically manipulated cells or organisms") which does not distinguish the claimed invention over the prior art. There is no evidence of record that the product made by the processes recited in claim 4 are any different than those made by other means. Due to applicant's amendment, claim 13 is included in this rejection as well. The amendment to claim 1 broadened the scope of the claim by no longer requiring direct contact between a neuron or neuronal area. Claim 13, drawn to intraperitoneal injection, is also taught by Penkowa.

3. Claims 1, 4, 13 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Giralt 2002 (Experimental Neurology 173:114-128, available online 25 February 2002).

This rejection stands for the reasons previously made of record. Briefly, Giralt teaches administration of MT-2 to mice that had suffered a cryolesion twice daily, by i.p. injection, for three or seven days (p. 115, first column, last complete paragraph). Although the reference does not teach measurement of neurite outgrowth, such a measurement is not required by the claims. The route of administration is one that applicant considers to be effective (specification, p. 4).

The arguments offered as to why Giralt does not anticipate independent claim 1 are the same put forth with respect to Penkowa. These have been addressed in detail above and for the sake of brevity will not be reiterated here. The prior art reference teaches administering the same compound (MT-2) to the same patient population (patients in need of treatment of head injury, recited in claim 17 and encompassed by claim 1) as in the present claims. The reference teaches administering for the same period of time that applicant has shown to be effective (over four days) and by a route that applicant has shown to be effective (i.p. administration). Claim 4 is rejected as it recites a product-by-process limitation ("wherein said MT-II is produced by chemical synthesis or by production in genetically manipulated cells or organisms") which does not distinguish the claimed invention over the prior art. There is no evidence of record that the product made by the processes recited in claim 4 are any different than those made by other means. Due to applicant's amendment, claim 13 is included in this rejection as well. The amendment to claim 1 broadened the scope of the claim by no longer requiring direct contact

between a neuron or neuronal area. Claim 13, drawn to intraperitoneal injection, is also taught by Giralt.

Again, as discussed at the interview with applicant's representative on 22 June 2009, if the claims were amended to include a step of measuring axonal outgrowth, they may be patentable over Giralt. However, with the exception of claim 29, no such amendment has been made.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, and 6-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkowa (2002. Journal of Comparative Neurology 444(2):174-189).

The reasons why claims 1, 4, and 13 are rejected as anticipated by Penkowa are set forth above. While the reference teaches administering a total of 17.5 ug Zn-MT-2 in saline per day, divided into three separate doses (p. 176 first paragraph), Penkowa does not explicitly teach that the solution has a concentration of "up to about 5 ug/ml" as recited in claim 6 or "about 5 ug/ml" as recited in claim 7. Additionally, Penkowa teaches that endogenous MT-1, transcribed off a transgene, is sufficient to reduce CNS degeneration but does not explicitly teach administering this protein as encompassed by claims 8 – 11, as the protein is endogenous to the transgenic mice.

It would have been obvious to one of ordinary skill in the art to adjust the concentration of MT-2 administered by Penkowa. Changing the concentration of a composition is not supportive of patentability (MPEP § 2144.05(II)(A)). As Penkowa teaches a method according to claims 6 – 7 that differs only in that the prior art does not disclose the actual concentration of the composition, and altering the concentration of the active ingredient would have been obvious to one of ordinary skill in the art, claims 6 – 7 are unpatentable over Penkowa. Note claims 6-7 are not drawn to the amount of MT-II administered, but the concentration of the solution used to administer. The motivation to alter the concentration of the active ingredient would be to find a volume of injection suitable for the patient.

It also would have been obvious to one of ordinary skill in the art to coadminister MT-1 recited in claims 8 - 9 along with MT-2, with a reasonable expectation of success. The motivation to do so would be to provide additional neuronal protection. It would be reasonable to expect success as Penkowa teaches that endogenous MT-1 also has positive effects on neural health. The reasons why claims 10 – 12 are included in this rejection are set forth in the previous office action.

This rejection stands for the reasons previously made of record. Applicant did not separately traverse the examiner's determinations that the limitations recited in claims 6 - 12 would have been obvious to one of ordinary skill in the art, but rather argued that Penkowa does not anticipate claim 1. As set forth in the rejection under 35 USC 102 above, the rejection of claims 1 and 4 stands, so the present rejection also stands.

5. Claims 1 and 3 – 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkowa (2002. Journal of Comparative Neurology 444(2):174-189) in view of FR 2813529, cited on IDS filed 13 December 2004.

The reasons why claims 1, 4, and 6 – 13 are anticipated by or obvious over Penkowa are set forth above. Briefly Penkowa teaches administration of MT-IIA is protective of neurons, and teaches compositions comprising MT-IIA. Penkowa suggests that metalliothioneins can be used in treating CNS diseases (p. 187 end of first column). However Penkowa used rabbit metallothionein, and does not teach administration of human MT-IIA as recited in claims 3 and 5.

FR 2813529 teaches compositions comprising human MT-IIA, which are on point to claims 3 and 5. However '529 publication does not teach administering the compositions such that target neurons or neuronal areas are exposed to the MT-IIA-containing compositions.

It would have been obvious to one of ordinary skill in the art to modify the methods of Penkowa to use the human MT-IIA taught in '529 publication, with a reasonable expectation of success. The motivation to do so would be to ensure less of an immune response when treating human patients. The artisan would be motivated to make this substitution, thereby arriving at the invention of claims 3 and 5, because the human MT-IIA sequence was known in the art and shown by '529 publication to be suitable for administration to humans, and because the artisan of ordinary skill would immediately understand that using a protein from a foreign species would increase the likelihood of an adverse immune reaction.

Applicant did not separately traverse the examiner's determinations that the limitations recited in claims 3 and 5 would have been obvious to one of ordinary skill in the art given the teachings of the '529 publication, but rather argued that Penkowa does not anticipate claim 1. Since claims 1 and 4 stand rejected as set forth above, this rejection stands as well.

6. Claims 1, 4, 6 - 13, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkowa (2002. Journal of Comparative Neurology 444(2):174-189) in view of Deguchi 2000 (Pharmaceutical Research 17(1):63-69) and Yoshimura 2001 (Proc Natl Acad Sci USA 98(10):5874-5879).

The reasons why claims 1, 4, and 6 - 13 are anticipated by, or obvious over Penkowa are set forth above. Briefly Penkowa teaches that MT-2, decreases 6-AN-induced degeneration of gray matter when administered peripherally. Penkowa also teaches that in normal animals, MT-2 does not cross the BBB, but that the reason why the drug reaches neural cells in this particular case is because of the BBB-disrupting effects of 6-AN (p. 186 first column). While Penkowa teaches intraperintoneal injection as recited in claim 13, the reference does not teach direct injection of the drug to a neuron or a neuronal area, which is also recited in claim 13 and does not teach direct exposure to neurites as recited in claim 28.

Deguchi teaches that basic fibroblast growth protein (also called bFGF) is generally excluded from the blood brain barrier. At p. 69 final paragraph Deguchi indicates that less than 1% of the injected dose reaches the brain, and concludes that in order for it to have therapeutic efficacy within the brain more of it will need to be delivered. One solution proposed by Deguchi

is to attach the bFGF to a BBB-transport molecule. However Deguchi does not teach administration of metallothionein.

Yoshimura teaches administration of bFGF by injection of a nucleic acid that encodes the protein into the brain. See for example p. 5875, fist column, last two paragraphs. The reference provides evidence that this method is sufficient to get the bFGF protein into the brain; see for example Figure 4. However Yoshimura does not teach administration of metallothionein.

It would have been obvious to one of ordinary skill in the art to modify the methods of Penkowa by directly administering the MT-2 within the brain, thereby arriving at the "direct injection" limitation claim 13 and the "directly exposed to neurites" limitation of claim 28. The motivation to do so comes from the prior art references themselves. Penkowa teaches that when the BBB is not disrupted, MT-2 does not cross this barrier. An artisan of ordinary skill would understand that this means the protein cannot have its therapeutic effect. The references by Deguchi and Yoshiumura, taken together, show that one solution to the problem of getting proteins excluded by the BBB into the brain is to inject them directly into the brain, thereby guiding the artisan of ordinary skill to perform the steps recited in claim 13, and resulting in claim 28 as well.

Applicant did not separately traverse the examiner's determinations that the "direct injection" limitation recited in claim 13 would have been obvious to one of ordinary skill in the art given the teachings of Deguchi and Yoshimura, but rather argued that Penkowa does not anticipate claim 1. Since claims 1 and 4 stand rejected as set forth above, this rejection stands as well.

7. Claims 1, 4, 6 - 13, 15, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkowa in view of Deguchi and Yoshimura as applied to claims 1, 4, and 6 - 13 above, and further in view of Asanuma (2002. Neuroscience Letters 327:61-65; available online 21 April 2002).

The reasons why claims 1, 4, and 6 – 13 are anticipated by or obvious over Penkowa are set forth above. Briefly Penkowa teaches administration of MT-IIA is protective of neurons, and teaches compositions comprising MT-II, which is either the same as or an obvious variant of MT-IIA. Penkowa suggests that metalliothioneins can be used in treating CNS diseases (p. 187 end of first column). While Penkowa does not teach administration within the brain in those

patients without a disrupted blood brain barrier, Deguchi and Yoshimura indicate that this is an effective way to get a drug that does not cross the barrier into the brain. However none of these references explicitly teaches a method of treating Parkinson's disease by administering metallothioneins as encompassed by claim 15.

Asanuma teaches that mice which lack both MT-I and MT-II are exceptionally susceptible to the toxic effects of 6-OH dopamine. See for example Figure 1, top panels. 6-OHDA is a chemical used to kill dopaminergic neurons, and administration of 6-OHDA is an art accepted animal model of Parkinson's disease. Asanuma teaches that the results indicate that both MT-I and MT-II have neuroprotective effects for Parkinson's (see p. 63 final paragraph), and suggest that the protective effects of these proteins are consistent with their known free-radical-scavenging roles. However Asanuma does not explicitly teach administering MT-2 for treatment of Parkinson's disease as recited in claim 15.

It would have been obvious to one of ordinary skill in the art to administer MT-2, as taught by Penkowa, for treatment of Parkinson's disease, as suggested by Asanuma. The motivation to do so would be to effectively treat the disease. It would be reasonable for the artisan of ordinary skill to expect success, as Asanuma teaches that the lack of MT-I and MT-II leads to increased likelihood of death of dopaminergic neurons, the cause of Parkinson's disease, in the presence of certain toxins. Additionally Asanuma teaches the free-radical scavenging properties of these proteins, and teaches how these properties would be helpful in treatment of Parkinson's. Deguchi and Yoshimura indicate that if a drug does not cross the BBB (as is the case with MT-2 in normal patients; see Penkowa), administering it within the brain can ensure that the drug reaches its target neurons.

Applicant did not separately traverse the examiner's determinations that treatment of Parkinson's disease as recited in claim 15 would have been obvious to one of ordinary skill in the art given the teachings of Asanuma, but rather argued that Penkowa does not anticipate claim 1. Since claims 1 and 4 stand rejected as set forth above, this rejection stands as well.

8. Claims 1, 4, 6 - 14, 16, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Penkowa in view of Deguchi and Yoshimura as applied to claims 1, 4, and 6 - 13 above, and further in view of Walsh (US Patent Application Publication 2002/0155170, published 24 October 2002, filed 30 November 2001, claiming benefit of a provisional application filed 30 November 2000).

The reasons why claims 1, 4, and 6 – 13 are anticipated by or obvious over Penkowa are set forth above. Briefly Penkowa teaches administration of MT-II is protective of neurons, and teaches compositions comprising MT-II. Penkowa suggests that metalliothioneins can be used in treating CNS diseases (p. 187 end of first column). While Penkowa does not teach administration within the brain in those patients without a disrupted blood brain barrier, Deguchi and Yoshimura indicate that this is an effective way to get a drug that does not cross the barrier into the brain. However none of these references explicitly teaches a method of treating Alzheimer's disease by administering metallothioneins as encompassed by claim 14 or treatment of motor neuron disease as recited in claim 16.

Walsh teaches that Alzheimer's disease (AD) is likely caused by a metallothionein disorder; see paragraphs [0118] – [0119]. Specifically, Walsh teaches that the plaques associated with AD result from free Cu and Zn ions, and that these plaques as well as the symptoms of AD will be ameliorated by metallothioneins. Walsh also teaches that familial amyotrophic lateral sclerosis symptoms worsen when metallothionein levels decrease (paragraph [0120]); this is a specific type of motor neuron disease. Walsh teaches and claims administration of a pharmaceutical composition which increases the amount of metallothioneins for treatment of Alzheimer's disease and the motor neuron disease familial amyotrophic lateral sclerosis, which is on point to instant claims 14 and 16 (see Walsh paragraph [0120] and claims 42 – 43). However Walsh does not teach administering MT-2 for treatment of Alzheimer's disease as recited in claim 14 or for treatment of motor neuron disease.

It would have been obvious to one of ordinary skill in the art to administer MT-IIA, as taught by Penkowa, for treatment of Alzheimer's disease and the motor neuron disease, as suggested by Walsh. The motivation to do so would be to effectively treat the diseases. Deguchi and Yoshimura indicate that if a drug does not cross the BBB (as is the case with MT-2 in normal patients; see Penkowa), administering it within the brain can ensure that the drug reaches its target neurons.

Applicant did not separately traverse the examiner's determinations that treatment of Alzheimer's or motor neurons disease as recited in claims 14 and 16 would have been obvious to one of ordinary skill in the art given the teachings of Walsh, but rather argued that Penkowa does not anticipate claim 1. Since claims 1 and 4 stand rejected as set forth above, this rejection stands as well.

Allowable Subject Matter

9. Claim 29 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach or suggest measurement of neurites after administration of the metallothioneins recited in claim 1.

Conclusion

10. No claim is allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. van Lookeren Campagne et al. 1999 Proc Natl Acad Sci USA 96:12870-12875. The reference teaches that transgenic animals overexpressing MT-I are protected from the effects of stroke, suggesting that administering this protein would be therapeutic in animals suffering from stroke.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
December 4, 2009